MSVA 099

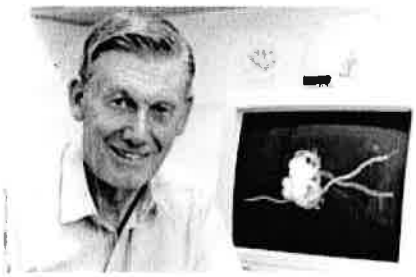
Australian Academy of Science - Science education
Interview with Professor Frank Gibson

Contents

Professor Frank Gibson, biochemist, was interviewed for the Australian Academy of Science's *Video Histories of Australian Scientists* program in 1993. The interview was conducted by Dr Max Blythe of the Medical Sciences Video-archive of the Royal College of Physicians and Oxford Brookes University in the United Kingdom. Here is an edited transcript of the interview.

You can order the videotape from us for $65.50 (including GST).

List of edited transcripts.



Finding something suitable to do

Frank, you were born in 1923 in Melbourne. Tell me about your family life.

My mother was of Scots and English extraction and my father of Irish extraction, and we were definitely working class. My father was trained to be a glazier originally, but after he came back from the First World War he worked for the Adelaide Steamship Company as a wharf labourer and eventually foreman stevedore, unloading coal ships.

That was a tough job.

It was. I remember that during the Depression he would sometimes work 72 hours at a time as the foreman. But we were very much shielded from that and I never felt the effects of the Depression very much at all. My mother held

the family together – I had two sisters, and we were all a very tightly knit family. We had no car, and I recall that the big events in my life were a pair of skates and a bicycle. I guess the fact that I don't have many memories of that time means we were very happy.

Four generations: a young Frank Gibson with his father, grandfather and great-grandmother.

What was going to school like for you?

I was a pretty mediocre student, I guess. As a very small student I got into trouble because I hadn't taken my homework books home for six months or something like that. Another time I got 22 per cent for algebra, but after a stern lecture from my father I got 96 per cent the next term. I really wasn't very worried about schoolwork.

I think my parents' idea was that I would become a white-collar worker rather than a labourer, so they encouraged me to become a draughtsman. I went off after primary school to a technical college for about two years, but it wasn't a great success. I was not a very good artisan, I'm afraid. I could never keep the drawing paper clean, I made an electric iron that didn't work, and all sorts of things like that.

At Collingwood Technical College, 1935.

The move into bacteriology

Then several people from the technical college went to work in the Bacteriology Department at Melbourne University, where Harold Woodruff was department head. Almost as an act of charity, I think, he would take in

boys from technical college, rather than high school, as laboratory technicians. A friend of mine went and then a few months later another opportunity arose, I went up for an interview and I got the job. I remember being asked what Sunday School I went to. Luckily, I said Methodist – I had gone there once – and it turned out he was a staunch Methodist. Whether that got me the job or not, at least it was the right thing to say. That was 1937: I started work at 14.

There is no question that somehow I had already become interested in science. I used to get and read a series which came out in parts, called *The Science of Life*, by Huxley, Wells and that crowd, and I managed to get a microscope (not much more than a toy) for which my sister tells me I used to pay a penny to get a drop of blood from her and a friend. But I don't know whether that's fact, fiction or family myth.

What kind of a world did you go into?

I thought it a very happy world. The department had almost a conveyor belt: as a technician you came in at the beginning, took the specimens down town to the Public Health Department, ran the messages and collected the lunches, and washed test tubes. When someone left, you would be promoted to plugging test tubes – and after six months you would become a very good judge of how much cotton wool to put in the neck of a tube. You moved on to the media room, making up bacteriological media, and then into either a teaching lab, helping prepare the materials for the classes and so forth – this was quite a big department for its day, teaching medicine, dentistry, agriculture, science – or one of the research labs.

Perhaps by luck, I was put into a research lab. That involved simple, routine laboratory manipulations, or setting the coal fire in the winter. I was working for Syd Rubbo, who later became head of the department. Adrien Albert was the collaborator in Sydney who even then used to send acridines to Melbourne for bacteriostatic testing and so forth.

After work we would go down and get fish and chips, and come back. It was a very happy place to work, because there were quite a few technicians, all fairly young and all doing courses – and in those days it didn't seem any hardship to do four nights a week at night school.

I was encouraged to start a Diploma of Chemistry in the Working Men's College, now the Royal Melbourne Institute of Technology. There were no biology courses; the idea was that you did chemistry. So I did chemistry I and chemistry II, a bit of scientific German, and maths and physics. But while I was doing chemistry II, I came off my bicycle and knocked all my front teeth out. So I had rather a traumatic year – for example, I couldn't use a pipette because it was too painful – and I failed chem II at technical college.

Jack of all trades: junior technician, university demonstrator and science

student

In about 1939, David Gray (Syd Rubbo's brother-in-law, a veterinary surgeon) was to start up the new Bacteriology Department in the University of Queensland and needed an offsider. One of the perks of the job was that they would pay fees and give time off, if necessary, for subjects in the university's night courses – you could do at least the first two years of a science course at night, over four years.

I was encouraged to apply for the job but once I was in Queensland I had the slight barrier of needing to matriculate. There was no way I could have matriculated to the University of Melbourne, but the University of Queensland went through all my papers and gave me my one term of scientific German as a language. And I had passed Leaving English, which was the matriculation English in those days at Melbourne, as part of the Chem Diploma course at the tech. Finally, the university decided that to matriculate I would have to do physics, maths and chemistry at Leaving level – which was very good, because they were the three subjects I knew most about – and then said that chemistry and physics would do. So I spent a year doing that. I went on to university after matriculating, and started chemistry, biology and so forth. That was once again four nights a week, I think, after work.

Was Bacteriology a good new unit to work in?

It was a pretty small show, only two of us. David Gray wasn't there very much (he was out at the Veterinary School) so I prepared the materials and did demonstrating to medical and science students – usually you wouldn't expect a junior technician to be demonstrating to them as I was. Later on we expanded, getting another technician so there were three of us in the department. We went like that for some time.

A strange war

While you were getting your matriculation, war was beginning. It proved a strange war for you.

It wasn't exactly my war. Firstly I went into the Volunteer Defence Corps, the Australian equivalent of 'Dad's Army'. I was put into the intelligence section, but that wasn't a great success because I could never remember the Morse Code and so communications were limited.

Some people were conscripted for service within Australia, although they were later used in New Guinea. Because my father had been in the AIF, the overseas force, and one of my best friends in Melbourne was in the Air Force and another was a Commando, I thought it would be a good idea to be in the Services. As a laboratory technician I was in a reserved occupation, but by some bureaucratic misdemeanour I was actually called up, conscripted. I was

put into the Brisbane showgrounds and as soon as I was there I thought, 'I'm in. This is it.' I sent my father a telegram asking his permission to join the AIF, he sent back his permission, and I was enrolled.

I didn't get into any of the more glamorous sections, because they said, 'Oh, you're a laboratory technician,' and I had to admit that. I ran dead in all the right tests they give you when you first go into the Army, but to no effect. I had to go into the Medical Corps, where they made me a stretcher-bearer. People are very heavy to be carried round, and I didn't like that much.

Then the university started trying to get me out. This developed into a major operation. I was writing letters saying (probably very foolishly) I wanted to stay in, and the university was writing, 'We want him back.' After a while I was hauled up before the officer commanding the Medical Corps in Queensland, and eventually I was sent out on leave. I spent the next six months or so, while they thought things over, in uniform but back in the Medical School. Then they threw me out altogether. I finished up with 286 days 'active service in Australia' – which was enough to get a War Service home.

Resuming work with acridines

So you were back at Queensland University. You prospered fairly well, but after year 2 you decided to go back to Melbourne.

Yes. I was getting 51 per cent all the time in my courses, because I used to go either surfing or bushwalking – which was almost unheard of in Queensland at the time. I used to walk in the rainforest of south-eastern Queensland and climb the mountains there. We went away practically every weekend, and I used to take a week off before the exams. These days, with continuous assessment, you couldn't do that, but it was absolutely wonderful even if I wasn't doing very well in my courses. I did get some decent marks in chemistry II, however, after Cec Williams (a friend who was a pharmacy lecturer up there) pointed out the error of my ways.

After four years, during which I had done first and second year science, I wanted to major in biochemistry and bacteriology. The bacteriology school in Melbourne had got even bigger since I had left it, so I went back to Melbourne and started to work there, becoming a senior demonstrator after a time. I spent two years studying while I worked – they let me do bacteriology I and II in the same year, which was quite good as I'd had enough years in bacteriology then to cope with that, and then biochemistry. I did reasonably well in those subjects, and then I got my BSc.

I became a junior lecturer for a while and then started to do a bit of independent research, back with the acridines. It had occurred to me that the acridine nucleus was very much like the riboflavin nucleus, and they might be acting as metabolic analogues. If I remember rightly, I was able to show there

was a correlation between how the substituents on the acridines resembled the flavin and the degree of inhibition of bacterial growth. I published that.

Actually, my first publication had been a little note in the *Australian Photographer*, some years before. Being interested in photography, I had taken a photograph of a wedding. It was very much underexposed and so I developed some concoction to intensify it. That first publication is completely lost – I've never seen it since. I do remember, though, that the editor insisted on removing the word 'wedding' and putting in 'a social occasion', as if there were something wrong about photographing a wedding.

When you were working with the acridines, was Rubbo still giving you his support?

Yes. I was doing some work in collaboration, but I was given a pretty free hand. Then I applied for an ANU scholarship, although there was still nowhere to do PhDs in Australia. At first my application was rejected because I didn't have an honours degree of any sort – just my BSc plus one research paper – but a couple of months later I got a letter out of the blue saying they'd thought it through again. I'm not quite sure of the background to that. Syd Rubbo might have been involved, and maybe Florey (who was in charge, essentially, of the PhD scholars who went to England). Anyway, there was great jubilation all round and the family were quite excited.

Actually, a sidelight which I haven't thought of for probably 40 years was that when the scholarship was announced, the Melbourne *Herald* said that 'Ralph Gibson' had been given it. Ralph Gibson was a well-known Communist in Melbourne, and my father was so irate that he marched me into the *Herald* office to demand a retraction.

A family move to Oxford

And so you went off to Oxford. By that time you had a wife to go with you.

Yes. I married my first wife, Margaret Burvill, in 1949, not long before my scholarship was announced. She was a Queensland graduate whom I had met briefly – I demonstrated to her – in Queensland. Then, when I came back to Melbourne, she was working in the Rubbo laboratory with Adrien Albert. She had done some very nice work on the motive action of 8-hydroxyquinoline, oxine, and had published quite a lot with Rubbo and Albert – much more than I had published. We did some work together on low-level resistance to streptomycin, which didn't add up to much in the end but was thought good enough for a note in *Nature*.

When we went over to Oxford, my wife cast around and inquired at the Dunn School and in Hinshelwood's physical chemistry laboratory. She was offered a job in the Dunn School but also she was offered a job with the possibility of

doing a DPhil in Hinshelwood's lab, and so she went to work there.

It must have been exciting to arrive in Oxford and meet Florey for the first time.

Yes. I remember very distinctly going in to see Florey. He explained that I was going to work over with D D Woods (which I knew already) and that he would take me over there. Then he explained the structure of the university, saying that I would have to become a member of a college before I went through the university. When he asked what college I would like to become a member of, being completely naive and knowing nothing about Oxford or colleges I didn't say 'Balliol,' or anything like that. I thought and said, 'Well, I'd rather like an old one.' 'Oh,' he said. 'My college is Lincoln, 1427. Will that do?' I said, 'I think it will do,' and so I became a member of Lincoln – not that I had much to do with Lincoln, which was mainly a conduit for getting money out of me. There was no Middle Common Room, I was married, so I lived out.

For a start we lived in Headington but later on we got a few rooms overlooking High Street, just opposite St Mary's, which was very good. It used to be an inn, apparently, and it had a nice big bow window, a little bearpit in the back, and a set of spiral steps you fell down to get downstairs – all the right things.

Of vitamins, pathways and bacterial mutants

What was it like to work with D D Woods?

Working for D D Woods was great. He was a great scholar and a wonderful supervisor. I thought we might not get on very well to start with, because soon after I arrived I said, 'Now, you won't mind if I take 10 days off to go skiing at Easter, will you?' He sort of looked at me and said, 'Well, I don't pay your salary,' turned on his heel and walked off. But he really was great.

June Lascelles and Bill Murrell were there, so there was quite an Australian and New Zealand connection, but for a while I could not say I felt completely at home. It seemed to me that whenever I'd go there, at about nine, I'd find people at work. Then, because it was in December–January, it would get dark at about three but it felt like midnight. And when I left, at half past five, people were still at work. We did settle into a good routine, but it seemed a bit foreign at the time.

What did you do for your DPhil?

D D Woods was interested in folic acid metabolism and function, and vitamin B12 function. Vitamin B12 and folic acid were thought to be concerned in the biosynthesis of the amino acid methionine, and I was put onto that project. Luckily, it worked out quite well and we found that serine was the source of the methyl for the methionine. It didn't have a great impact on the

scientific world. We had one short communication at a meeting, but D D Woods wasn't well and when I left the work it hadn't been written up. It wasn't published till seven years later, by which time everyone knew that serine was the source. But the joy of doing it was all that really mattered.

That DPhil work says a lot about the rest of your career. It sets marks. You were using bacterial mutants, weren't you, coming in on a new wave of discovery.

Yes. It was the era when studies on bacterial nutrition had led to the idea of a way to work out pathways, in particular with tryptophan in the case of bacteria and several pathways in *Neurospora*. Beadle and Tatum had shown that it seemed that when you got a mutation in a gene you blocked a single enzymic step, and also that if that step was blocked, then the intermediate preceding the step might pile up and you could isolate and identify it. Then Lederberg's work with bacterial mutants had shown a further way to study pathways, which now were starting to be built up. Tryptophan was one of the first ones. This was very exciting.

I was interested in vitamin B12 function and folic acid function as well as the actual pathway, and I found that you could either grow the organisms in very limiting vitamin or find some mixture of compounds that replaced the vitamin. So you could make vitamin-deficient cells by having a mutant which could not form that vitamin. Then you could add the vitamin and see whether it functioned and so forth.

That was a terrific manipulation of metabolism. You really liked bacterial cells, I think. Perhaps that stemmed from your bacteriology laboratory days.

Well, in Oxford I was exclusively working with cell suspensions – growing up whole cells, washing them and using them. I had very little experience before I finished my DPhil with smashed cells and enzyme preparations. That came later.

An interesting DPhil oral

After you wrote the thesis up, you were examined by an internal examiner, Rudolph Peters, and an external examiner, Hans Krebs. I believe Krebs was late.

Yes. I got all dressed up in subfusc – white bow tie, dark suit and everything – but when I turned up at about 9 o'clock for the appointment, I got a message that Krebs had been delayed and wouldn't arrive till about 11. Needing something to read for the next couple of hours, I walked in to the lab of June Lascelles, who had a row of green Penguin mysteries on her shelf. But when I pulled one out at random, it was called *Death in a White Bow Tie*. I threw it down and walked out.

The oral was interesting. I became an observer of the polite interaction between Krebs and Peters: very much a case of 'After you,' 'No, after you.' Peters came in with bits of paper stuck out all the way through the thesis, to ask me questions. That gave me a shock, but it was fairly obvious after a short time that neither of them had worked in that field, so in a sense I was on top.

Wasn't Krebs was a bit mystified by what you had achieved on the biochemical pathway, looking at intermediates without viable manometry?

Yes. When Krebs handed back my thesis as he left, he said, 'All this without manometry.' Oddly enough, during the next few months while Margaret finished her DPhil, I did learn manometry in the microbiology lab – Bill Murrell did quite a lot of it.

One Saturday morning: an unexpected insight into pathways

You re-established your link with Melbourne, which had been an important place for a long time.

Yes. I enjoyed Oxford and developed good links there. But some time before I was due to leave, I had two letters. One was from Syd Rubbo, saying that Frank Fenner was intending to offer me a job but that he also wanted to offer me one. (These were the halcyon days when you were offered jobs.) Frank Fenner was offering me a job as a Fellow in the John Curtin School of Medical Research, in Canberra; Syd Rubbo's job was back in Melbourne as a senior lecturer. Because I like teaching and also because virology – which is what Frank Fenner's department was concerned with – was a bit of a foreign field for me, in 1953 I went back to Melbourne.

You went back on to related pathways. Tell us about your 'one Saturday morning' experiment.

Well, it did things, even if they were all the wrong things. I was interested in one-carbon transfers, having been working with that in Oxford. I had an idea that anthranilic acid could be converted to indole, which is a step on the tryptophan pathway known because of the use of mutants. That ostensibly is an addition of one carbon atom. In Oxford I did an experiment where I added serine to anthranilic acid and showed that indole was formed. So I thought, 'Ah, I will go with this. I can go back and work on the same general area, studying one-carbon transfers.'

When I did the same sort of thing in Melbourne and did the controls, I found that if I used glucose and ammonia I got just as much indole formed as if I had serine present. That showed me I never used the library, or I would have discovered that that was not the way indole was made – Yanofsky had shown some time earlier that it was made by the addition of a five-carbon ribose

fragment to anthranilic acid. But the interesting thing was that it meant that by incubating glucose and ammonia with a mutant that was blocked after indole, you could get indole formed. It allowed you to study the whole pathway. You could look for mutants with other compounds being produced.

Was this drawing on your early work on antibiotics?

Yes. Initially I was interested in whether antibiotics inhibited any steps in the pathway. From the early work on the acridines I was very interested in the motive action of antibiotics, and also the book by Work and Work on the basis of chemotherapy had a big influence on me. We spent quite a lot of time mucking around with antibacterial action. It didn't really get very far – it was a diversion, I suppose – but it did lead us on to really thinking about the biochemistry of the pathway. We then started to isolate mutants which were forming various compounds. We would generate the mutants, in the sense that you treat them with a mutagen and then look for mutants which will grow on some media and not on others. It was fun, especially in those days when there were plenty of novel mutants to be found.

Bacteriology Department, University of Melbourne, 1958.

The dramatic discovery of chorismic acid

Tell me more about that way into the pathway, Frank.

We were interested in the early part of the pathway. There had been a lot of work done by Davis and Sprinson in two groups working in the United States, and the pathway was starting to be established. It was known that there was a so-called common pathway which led from carbohydrate and branched out to three different amino acids, phenylalanine, tryptophan and tyrosine, and then possibly to para-aminobenzoic acid and possibly to folic acid. The big mystery was where the pathway branched.

We started to study the pathway, using mutants blocked at various points near where the branch-point might have been – eventually deciding that if we could make a multiple mutant, blocked all the way round the branch-point compound, that should pile up. In theory it wasn't possible to do that – the reasons get a bit complicated – but we did the experiment the best way we could and found that a compound did pile up. We extracted the compound into

ether, looked at the spectrum and knew we had a new compound being formed. Great jubilation.

Was the discovery of that the greatest moment of all?

Yes. There have been some good ones, but seeing that was one of the best because it came in so dramatically. One minute it wasn't there, and next minute there was the spectrum in front of your eyes.

I remember very distinctly that Margaret was the one who actually ran the spectrum. Soon after that she became ill and had to leave the lab, and then I spent a lot of time trying to isolate the compound. I wasted a tremendous amount of time. Because no-one had ever found it before and everything, I thought it must be so labile that it had to be treated very delicately, very gently, or it would break up. So I ran all sorts of exotic columns. I remember doing some very dangerous things like, in a very poorly ventilated room, running columns of powdered sucrose and ether. Safety committees would never let you do things like that now.

Anyway, I lived through that, and eventually found that you could put the compound onto ion exchange columns and get it off, provided you did things very quickly and cold, even though it was unstable. It spontaneously broke down into one of the intermediates in phenylalanine biosynthesis and also into para-hydroxybenzoic acid. Getting this compound opened up a Pandora's box: we could look at the pathway to the three amino acids and so on. We knew para-aminobenzoic acid (PABA) probably came from that compound, and we were able to show that. Then we started to look at other compounds also, and later in Canberra we did a lot more.

Why was the compound called chorismic acid? I must say I love that name.

My father-in-law, a clergyman in the Church of England, was a Greek scholar. I wrote to him outlining the situation – that we had a pathway and a branch-point – and he suggested several words from a Biblical quotation which I think has to do with St Barnabas and the young St Luke. That they 'parted asunder' was the important thing, and he suggested 'apochorismate' or 'chorismic' or words like that. I chose 'chorismic', because 'apo' has chemical connotations and one could confuse it.

And it is in the biochemistry literature for all time.

Yes, I assume so. It would be a bit hard for anyone to pirate it now.

Who'll come a-moving to Canberra with me?

You were given a Personal Chair in Melbourne and you built up a really significant team, didn't you?

One of the great things at that point was the people I had working with me. I had some fantastic graduate students – Margaret was working with us and there were several others who have made names for themselves, such as Jim Pittard, later head of the Microbiology Department in Melbourne University, Dick Cotton, who is now deputy director of the Murdoch Institute in Melbourne; Ian Young, who is head of the Division of Biochemistry and Molecular Biology in the John Curtin School of Medical Research, at the ANU; and Graeme Cox, who has been working with me for about 35 years. He is now my boss, a professor in the ANU. Several of those people have given Biochemical Society named lectures and so forth. It was a great team.

But then you got a chance to change jobs. How did that come about? And I believe your research family wanted to move with you to Canberra.

I got a summons from Sir Hugh Ennor, whom I knew only by name as head of the Biochemistry Department at the John Curtin School, although I think he was the Deputy Vice-Chancellor at the ANU at that time. He asked if he could see me at 'Menzies Hotel, breakfast,' and I went along, with no idea what this Sir Hugh Ennor could want with me. He said they were trying to fill the Chair of Biochemistry in the John Curtin School. Would I let my name go forward? I had never thought of myself as anything but a bacteriologist, so to have someone calling me a biochemist gave me quite a turn.

I thought about it, and I came up. The decision was not easy, because my wife was ill and anyway I was settled in Melbourne. But I decided to let my name go forward, and I was offered the job and took it. When I went back to the lab I said, 'I've been offered this job in Canberra, and they say that I can bring someone with me if I want to. Does anyone want to go?' I think five people came, which was great because it meant the work could just go on as before. We had just a short problem of setting up and then away we went. I must say that I have never regretted coming to Canberra. It's a very good place both for work and for play.

In Canberra your work then flooded out into some quite exciting areas..

That's right. One of the good things about the job here was that, as Hugh Ennor pointed out to me, the department was very small. Although there were at that time four research groups including us and we were very crowded, we had a good laboratory manager and the head of such a small department virtually had no teaching. You could just carry on at the bench, really, which was great.

Graeme Cox and Ian Young were here, and we found that chorismic acid was the precursor of ubiquinone, one of the compounds involved in electron transport. We started to study the biosynthesis of that by isolating mutants, isolating the compounds and so forth, and eventually Ian Young took that on.

With some radioactive tracing experiments by Graeme Cox, we found that chorismic acid was also the source of vitamin K, the source of which was completely unknown.

Also, we started working again on phenolic compounds – dihydric phenols – that were produced by mutants. Jim Pittard (who was originally an MSc student) had looked at a number of them while we were in Melbourne, but although a lot of them were produced we could not work out what they were for. Jim had shown the compound 2,3-dihydroxybenzoic acid, but now Graham Cox identified 2,3-dihydroxybenzoylserine and eventually showed that the important compound was one which we called enterochelin but is now known in the literature as enterobactin. And that turned out to be important in iron transport in bacteria. So not only were we able to work on these compounds but in the case of the iron-binding compounds we were able to postulate a pathway for the uptake of iron, using these compounds, and in the case of ubiquinone to postulate a mechanism of action – how it worked in two particular places in the pathway of electron transport. That time was not only productive, it was very exciting.

Didn't you then make a new departure, getting into bacterial genetics in a big way?

Yes. That had arisen just before we left Melbourne. Jim Pittard went away to work with Adelberg in the States, and came back imbued with the new bacterial genetics. Then we started not only to isolate mutants but to map them and carry out transductions to purify the mutants we had. I think since that time we have taken up with all the new techniques that have arisen in bacterial genetics, right up to site-directed mutagenesis and PCR and so forth.

Oxidative phosphorylation

Becoming interested in oxidative phosphorylation, as we did next, was a bit of a shock because it was a field we knew nothing about – an obviously very controversial field and one which occupied some of the big biochemists of the time. The interesting thing was that until almost 1970 very few had used *E. coli*, in particular, or any bacteria, to study oxidative phosphorylation in detail. I think the reason was firstly that all the dominant figures in the field were eukaryotic specialists, and secondly that those people who had done a little bit of work on oxidative phosphorylation in bacteria had shown that the so-called P/O ratios are very low, therefore the organisms are pretty inefficient – and who'd want to look at those anyway?

We tackled it from a different angle. We had looked at ubiquinone mutants, and these had deficient respiration, and we had a lot of mutants which were deficient in respiration but were not ubiquinone-deficient. Therefore, there was something else wrong with them. Examining some of those, we found that some of them lacked ATP-ase activity and so we were led to look at the

ATP-ase. Virtually nothing had yet been done about ATP-ase in *E. coli* or bacterial cells, although quite a lot was known in the mammalian system and it was known to be a complex, with many subunits. So we started to isolate various mutants and identified, I think, seven out of the eight genes that were concerned with this process. We then started to work on function.

To bring that right up to date: Graeme Cox developed a theory which suggested that the function of ATP-ase, or the mechanism of action, was one in which there was a rotational model, with the ? and ? subunits at the top and a central rotating core inside. This was novel. A rotating model had been mentioned by Boyer, but that was rotating the whole ? and ? subunits. That model – which we are still working on – seems to be holding up even now, although getting definitive proof is very difficult.

That really is an enzyme complex – classical, and one of the most important of all.

Yes, and I think that the bacterial work that we did – and that a lot of others have done since then, because it became fashionable to work on *E. coli* and quite a number of labs took that up with oxidative phosphorylation – has given a lot of insights into the process which had been used by people in the eukaryotic field to work on their aspects of it. *E. coli* is a wonderful laboratory tool because you can work so quickly and easily with it and get results.

At the John Curtin School of Medical Research, 1971.

Molecular modelling

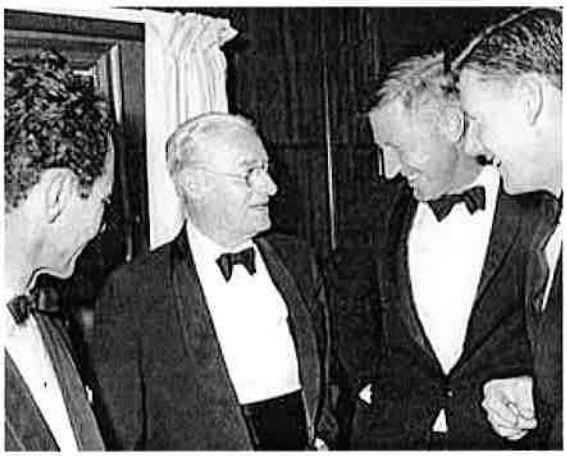
I think you're still enjoying your research, perhaps studying your great stocks of mutants. Or is your work now mainly administrative?

Certainly I have thousands of mutants, but I don't do any lab work now – nor any administrative work at all. I spend most of my time in front of a computer.

When Robin, my second wife, spent a year with me back in Oxford, she gave me a BBC microcomputer – 32K and a television screen – for my 60th birthday. After we returned to Canberra I started to play with that, using it to set up the computing for her business as a solicitor. (Having a small child, she was working from home.) I became further interested, starting to use PCs and then Macs, and so when I retired I thought, 'Well, the best thing I can do to further the work of the group is to go into computing.' I was encouraging people to go into molecular graphics; we bought a workstation; and now that we have state-of-the-art software and a good workstation I spend most of my time doing molecular modelling and working as a Visiting Fellow – along with a few committees of various sorts and so on.

Molecular modelling must be wonderful. Isn't it time-consuming, though?

Very time-consuming. I realise now that it is as much experimental science as any other, especially when you are modelling compounds, proteins, for which a structure is not known by X-ray crystallographic techniques. You can drag in files and put structures of known proteins up on the screen, but when you are dealing with proteins where you don't even know whether it's an alpha helix or beta strand, then it gets more difficult – although if you are modelling membrane proteins it is not so bad, because you can assume that they are going to be alpha helical. So we model parts of the ATP-ase complex and also model the various mutants and see what happens.



From left: Dr Harry Rosenberg, Lord Florey, Professor Bede Morris and Frank Gibson (taken about 1975).

Home and away: 'doing the next thing'

You have done a lot of overseas travel, making contacts with many people in your field and playing an ambassadorial role. And some very exciting people have come here to work with you. Has this been an important part of your life?

It has been quite an important part, arising mainly from the times spent in Oxford. The second time, in 1982–83, was under rather different conditions from the first, because I was by then a Fellow of Lincoln.

You got value from Lincoln that time, did you?

Very much so, yes. It was a great experience, quite useful – and certainly different from being a student and not seeing the college. I went to the main department a fair bit, whereas in the early days contact with the main department was not encouraged. (So I used to sneak into the library late in the afternoon and get the jam and bread they had left, I remember. But that's another story.) I met Norman Heatley over there, among others. I saw quite a lot of Henry Harris during lunchtimes at Halifax House, and I worked with Joel Mandelstam.

There have also been visits to the States, where I made some very firm friends, and probably as a result we've had people like Charlie Yanofsky out here, Ed Reich and Fred Crane, and Simon Silver. Quite a few people have come out to work in the lab and it's been very valuable.

Frank, it's been marvellous to talk with you about all these things. What a career.

Well, it just evolved – we used the techniques that came along, as they applied to our problem. My life has been just a matter of doing the next thing. I never feel I have had to make any serious choices. It's been as simple as that, and it's been enjoyable.

And it shows. Thank you very much.

[**Home** | **Contacts** | **Publications** | **Search**]
